REMARKS

Claims 1, 3, 4 and 6 are pending in this application. Claim 5 has been canceled without prejudice or disclaimer. Claims 1, 4 and 6 have been amended.

Claim 1 has been amended to place it in proper U.S. form and to incorporate the limitations of claim 5, now cancelled. Support for the amendment is found in the specification as-filed, for example, at page 21, line 15, to page 22, line 25, and in the Examples. These amendments are for the sole reason of advancing prosecution. Applicants, by canceling or amending any claims herein, make no admission as to the validity of any rejection made by the Examiner against any of these claims. Applicants reserve the right to reassert any of the subject matter canceled herein or the original claim scope of any claim amended herein, in a continuing application.

Claim 6 has been amended to correct claim dependency in view of the cancellation of claim 5.

No new matter has been added.

In view of the remarks set forth below, further and favorable consideration is respectfully requested.

I. Rejection of claims 1 and 3-7 under 35 U.S.C. § 103(a)

The Official Action states that claims 1 and 3-7 are rejected under 35 U.S.C. §103(a) as being unpatentable over Miranda et al. (U.S. Patent No. 5,656,286), in view of Hoffman. In particular, the Official Action in relevant part states that:

> Miranda teaches "a transdermal drug delivery system "wherein a blend of polymers is utilized to affect the rate of drug delivery from composition...adjusts the solubility of the drug in a polymeric adhesive system formed by the blend, affects the maximum concentration of the drug in the system, and modulates the delivery of the drug from the composition and through the dermis" (Col. 1, lines 24-34)." See page 10 of the Official Action.
>
> Applicants argue that neither the Miranda et al. nor the Hoffman reference, taken alone or in combination, disclose all of the limitations of the presently pending claims, as required by *In re Wilson.* See page 3 of the Official Action.
>
> This is not persuasive because one of ordinary skill in the art would have found it obvious to combine the styrene-isoprene-styrene block co polymers as rubber-based pressure-sensitive adhesives and butyl methacrylate is copolymerizable with methacrylic acid and dimethylaminoethyl methacrylate as suggested by Miranda, with the styrene-isoprene=styrene (SIS) block colpolymer of 2-ethyl-hexyl acrylate (2-EHA) and vinyl acetate (VA), and the acrylic resin of dimethylaminoethylmethacrylate and neutral methacrylate (EUDRAGIT E 100 from ROHM), as suggested by Hoffman, and produce the instant invention. See page 4-5 of the Official Action.

Applicants respectfully traverse the rejection of claims 1 and 3-7 for the reasons of record, and as supplemented herein. The cited references do not establish a *prima facie* case of obviousness against the presently pending claims. To establish a prima facie case of obviousness, three requirements must be satisfied. First, as the U.S. Supreme Court recently held *KSR International Co. v. Teleflex Inc.,* 550 U.S. 398 (2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether

there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." (*KSR,* supra, at 417). Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.,* 18 USPQ 1016, 1023 (C.C.P.A 1970). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

A. The Presently Claimed Invention

The presently pending claims as exemplified by presently pending independent claim 1, are directed to:

> A patch, comprising:
> a backing layer; and
> an adhesive layer disposed on the backing layer, the adhesive layer comprising a drug and an adhesive base agent comprising
> a styrene-isoprene-styrene block copolymer,
> 2-ethylhexyl acrylate – vinyl acetate copolymer, wherein the weight ratio of the content of the styrene-isoprene-styrene block copolymer to 2-ethylhexyl acrylate – vinyl acetate copolymer is from 1:1 to 9:1,
> a basic nitrogen-including polymer comprising a basic nitrogen and having no adhesion properties at normal temperature, the basic nitrogen-including polymer being selected from the group consisting of methyl methacrylate – butyl methacrylate – dimethylaminoethyl methacrylate terpolymer, and polyvinyl acetal diethylamino acetate, and

an organic acid selected from the group consisting of acetic acid, sodium acetate and citric acid.

Dependent claims 3, 4 and 6 each incorporate the features recited in independent claim 1, and further recite the features of: the solubility of the drug in water as being 1% or less; the drug, pergolide; and the use of an alicyclic saturated hydrocarbon-based tackifier in the adhesive layer.

Moreover, Applicants point out that the data shown in Tables 1-4 on pages 34-37 of the present specification demonstrates the unexpectedly superior results achieved by the presently claimed patch formulations as compared to patch formulations lacking one or more of the copolymers recited in the presently pending claims, and therefore, the present claims are non-obvious over the applied references.

B. The Teachings of the Miranda et al. Reference

The Miranda et al. reference describes "a transdermal drug delivery composition wherein a blend of polymers is utilized to affect the rate of drug delivery from the composition." *See* Miranda et al., column 1, lines 26-28.

C. The Teachings of the Hoffmann Reference

The Hoffmann reference describes "a novel therapeutic system with active substance depot for the administration of the active substance." *See* Hoffmann, column 2, lines 37 and 38.

D. No prima facie Case of Obviousness Has Been Shown

Neither the Miranda et al. nor the Hoffmann references, taken alone or in combination, describe all of the limitations of the presently pending claims, as required by *In re Wilson*. Neither the Miranda et al. nor the Hoffmann references either taken alone or in combination describe the weight ratio of the content of the styrene-isoprene styrene block copolymer to the content of the 2-ethyl-hexyl acrylate vinyl acetate copolymer, respectively; and wherein the weight ratio of the content of the styrene-isoprene-styrene block copolymer to the 2-ethylhexyl acrylate–vinyl acetate copolymer is from 1:1 to 9:1.

Miranda et al. only describe each monomer of methyl methacrylate, butyl methacrylate and dimethylaminoethyl methacrylate. Miranda et al. do not describe a combination of monomers consisting of 2-ethylhexyl acrylate–vinyl acetate copolymer and methyl methacrylate–butyl methacrylate–dimethylaminoethyl methacrylate terpolymer. In addition, Miranda et al. do not describe using 2-ethylhexyl acrylate–vinyl acetate copolymer and a basic nitrogen-including polymer together.

The Hoffmann reference describes patch formulations containing separate and distinct layers. In particular, the Hoffmann reference describes patch formulations which contain an active substance distribution device (i.e., a reservoir matrix layer) and a separate and distinct fixing device (such as, a porous pressure sensitive adhesive layer). The Hoffmann reference does not describe the combination of components in a single layer of the embodied patch formulations as required by presently pending claim

1. Further, the Hoffmann reference fails to describe the specific layer structure of the patch formulations as recited in presently pending claim 1.

Further, the Hoffmann reference ***teaches away*** because Hoffman requires patch formulations where the layer structure and the combination of components in the layer(s) are different from those recited in the presently pending claims. The Hoffman reference describes "the active substance delivery control device as a reservoir matrix having one or more discrete active substance depots arranged in a spatially defined manner with respect to one another and having a higher active substance concentration than in the reservoir matrix" (See col. 2, lines 46-51). The Hoffman reference clearly teaches a patch formulation in which the drug is kept in a depot separate from the adhesive layer. Therefore, the Hoffmann reference does not describe the combination of components in a single layer of the embodied patch formulations as required by presently pending claim 1.

In addition, neither the Miranda et al. nor the Hoffmann references, either taken alone or in combination, describe the inclusion of an organic acid selected from the group consisting of acetic acid, sodium acetate and citric acid in their respective patch formulations. Therefore, neither the Miranda et al. nor the Hoffmann references, taken alone or in combination, disclose all of the limitations of the presently pending claims, as required by *In re Wilson*.

There is no suggestion in the art to modify the combination of references to achieve the patch formulation of the presently pending claims with the specific

components in their recited ratio. Accordingly, a *prima facie* case of obviousness has not been established.

E. Unexpected Results Overcome *Prima Facie* Case

Even if the Examiner continues to assert that a *prima facie* case of obviousness has been shown, Applicants provide evidence of unexpected results of the claimed composition to rebut the assertion of a *prima facie* case of obviousness.

With regard to the Declaration by Kazunosuke Aida filed December 19, 2008, the Examiner asserts that

> Both prior art references teach polymers for the same purpose, i.e., adhesion and cohesion. If one of ordinary skill in the art uses the polymers of each reference singly, the amount of the polymers would be higher to get the same adhesive or cohesive effect. When combining the polymers of the two references, one of ordinary skill in the art will not use the same (high) ratio he/she used when using the polymers of just one reference, i.e. one of ordinary skill in the art would adjust the amount of the polymers in order to achieve the desired adhesive/cohesive effect. It would be well within the scope of routine optimization, when the polymers of Miranda and Hoffman are combined, to modify and adjust the ratio of the polymers (SIS and 2-EHA-VA). The data in Tables 1-4 on pages 34-37 have been fully considered but is not unexpected or surprising in light of the combination of Miranda and Hoffman and the expected routine optimization following the combination.
>
> The weight ratio of the content of the SIS block copolymer to 2-EHA-VA copolymer is a result effective variable that can be optimized to achieve the desired adhesion. The workable ranges or the ratio that achieve the recognized result (adhesion) may be optimized during routine experimentation. Please see MPEP 2144.05 and *In re Antonie,* 559 F.2d 618, 195 USPQ 6 (CCPA 1977).

Applicants bring the Examiner's attention to the unexpectedly superior properties of the presently claimed matrix outlined in Tables 1-4 on pages 34-37 of the instant

specification which demonstrates the unexpectedly superior results achieved by the presently claimed patch formulations as compared to patch formulations lacking one or more of the copolymers recited in the presently pending claims. In particular, Examples 1-3 summarized in Table 1 and Examples 4-7 in Tables 3-4 show adhesion and cohesion properties for compositions containing the presently claimed components. Comparative Examples 1-22 in Tables 1-4 show adhesion and cohesion properties for compositions lacking at least one of the components of the presently claimed formulation. ***The data clearly shows superior patch properties, when compared to the patch properties for compositions lacking at least one of the claimed components***.

While the Examiner included remarks with regard to the cohesive/adhesive effect of the combination of the polymers in the patch formulation, the Examiner did not comment on the unexpectedly superior skin permation rates of the patch formulation of the presently pending claims. Applicants bring the Examiner's attention to Tables 1-4 at pages 34-37 of the presnt specification (also stated at paragraph 4 of the expert's declaration of Kazunosuke Aida filed December 19, 2008), which demonstrate unexpectedly superior results achieved by the presently claimed patch formulations as compared to patch formulations lacking one or more of the copolymers recited in the presently pending claims. In particular, Examples 1-3 summarized in Table 1 and Examples 4-7 in Tables 3-4 show drug permeation rates per unit area of skin and adhesion and cohesion properties for compositions containing the presently claimed components. Comparative Examples 1-22 in Tables 1-4 show drug permeation rates

for compositions lacking at least one of the components of the presently claimed formulation. ***The data clearly shows superior skin permeation rates and patch properties, when compared to the drug permeation rates and patch properties for compositions lacking at least one of the claimed components***.

Accordingly, the results outlined in Tables 1-4, on pages 34-37, of the instant specification show unexpectedly superior results for the presently claimed compositions. Morevoer, there is ***no*** teaching or suggestion in the cited combination of references that one of ordinary skill in the art would have had a reasonable expectation of successfully combining the teachings of Miranda et al. with the teachings of Hoffman et al. to devise the claimed unexpectedly superior patch.

Accordingly, nothing in any of the applied references, taken alone or in combination, renders claim 1, 3, 4 and 6 obvious withinin the meaning of 35 U.S.C. §103. Thus, Applicants respectfully request that the Examiner reconsider and withdraw the present rejection.

II. Provisional Rejection of Claim 1 under the Judicially Created Doctrine of Obviousness-Type Double Patenting

The final Official Action states that claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3-11 of copending U.S. Patent Application Serial No. 10/526,065.

The Examiner asserts that although the conflicting claims are not identical, they are not patentably distinct from each other. The Examiner notes that the instant claims are directed to a patch comprising a backing layer and an adhesive layer that is

compounded with a drug and an adhesive base agent. The Examiner asserts that the claims of the copending U.S. Patent Application No. 10/526,065 also describe a patch comprising a backing layer and an adhesive layer compounded with an adhesive agent and pergolide.

It is submitted that present claims 1, 4 and 6 are patentably distinct from the claims of copending U.S. Patent Application No. 10/526,065. With regard to claims 1, 4 and 6 of the instant application, all of claims 1, 4 and 6 are directed to a patch, comprising: a backing layer; and an adhesive layer disposed on the backing layer, the adhesive layer comprising a drug and an adhesive base agent comprising a styrene-isoprene-styrene block copolymer, 2-ethylhexyl acrylate – vinyl acetate copolymer, wherein the weight ratio of the content of the styrene-isoprene-styrene block copolymer to 2-ethylhexyl acrylate – vinyl acetate copolymer is from 1:1 to 9:1, a basic nitrogen-including polymer comprising a basic nitrogen and having no adhesion properties at normal temperature, the basic nitrogen-including polymer being selected from the group consisting of methyl methacrylate – butyl methacrylate – dimethylaminoethyl methacrylate terpolymer, and polyvinyl acetal diethylamino acetate, and an organic acid selected from the group consisting of acetic acid, sodium acetate and citric acid.

Claims 1 and 3-11 of copending U.S. Patent Application No. 10/526,065 do not recite the specific combination of components in the adhesive layer that are required by pending claims 1, 4 and 6 of the instant application. Accordingly, present claims 1, 4 and 6 are patentably distinct from claims 1 and 3-11 of copending U.S. Patent Application No. 10/526,065. The Examiner is respectfully requested to withdraw this

rejection of pending claims 1, 4 and 6.

If the Examiner continues to assert that a *prima facie* case of obviousness-type double patenting has been shown, Applicants respectfully request that the Examiner hold this rejection in abeyance until such time as the Examiner indicates there is successful resolution of the claim rejections noted above. Applicants, at that time, will either address the rejection or cancel any conflicting claims in copending U.S. Patent Application No. 10/526,065.

CONCLUSION

Applicants submit that the application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is welcomed to telephone the undersigned attorney if she has any questions or comments.

In the event this paper is not timely filed, Applicants hereby petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

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